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(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Fumihide NISHIO

Application No.: 10/501,671

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Art Unit: 1651

For: **HIGH-CONCENTRATION PREPARATION OF
SOLUBLE THROMBOMOIDULIN** Examiner: S. R. Macauley

VERIFICATION OF TRANSLATION

The undersigned hereby declares the following:

That I am knowledgeable in Japanese and English. That I have reviewed the partial English translation of JP 2002-009951 and verify that the attached document is an accurate translation thereof.

All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. Further, these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

March 26, 2010

Date

M. Iwamura

Signature

freeze-dried preparation obtained by making a combination of: the soluble thrombomodulin-containing freeze-dried preparation listed in the column of composition in Table 5 obtained in the same manner as in Example 2-14, except that Polysorbate 80 was not added in the additive solution; and an ampule aseptically filled with 1 mL of solution containing 10 mg of benzyl alcohol in 1 mL of water for injection as a dissolving aqueous solution (just like the above description, Example 2-31-1 was prepared).

Example 2-32

A kit preparation of a soluble thrombomodulin-containing freeze-dried preparation obtained by making a combination of: the soluble thrombomodulin-containing freeze-dried preparation listed in the column of composition in Table 5 obtained in the same manner as in Example 2-14, except that Polysorbate 80 was not added in the additive solution; and an ampule aseptically filled with 1 mL of solution containing 5 mg of benzyl alcohol in 1 mL of water for injection as a dissolving aqueous solution (just like the above description, Example 2-32-1 was prepared).

Example 2-33

A kit preparation of a soluble thrombomodulin-containing freeze-dried preparation obtained by making a combination of: the soluble thrombomodulin-containing freeze-dried preparation listed in the column of composition in Table 5 obtained in the same manner as in Example 2-14, except that Polysorbate 80 was not added in

the additive solution; and an ampule aseptically filled with 1 mL of solution containing 5 mg of chlorobutanol in 1 mL of water for injection as a dissolving aqueous solution (just like the above description, Example 2-33-1 was prepared).

Example 2-34

A kit preparation of a soluble thrombomodulin-containing freeze-dried preparation obtained by making a combination of: the soluble thrombomodulin-containing freeze-dried preparation listed in the column of composition in Table 5 obtained in the same manner as in Example 2-14, except that Polysorbate 80 was not added in the additive solution; and an ampule aseptically filled with 1 mL of solution containing 2.5 mg of chlorobutanol in 1 mL of water for injection as a dissolving aqueous solution (just like the above description, Example 2-34-1 was prepared).

Example 2-35

Each 1 mL aliquot of sample solution was dispensed into one chamber of a two-chamber syringe (manufactured by ARTE) instead of the sterile vial in the preparation of the sample solution in Example 2-1. They were subjected to the freeze-drying step (under the same freeze-drying conditions as those of Example 2-1) in the order of: plugging with a middle stopper by half → freeze-drying → nitrogen-filling → plugging with the middle stopper. Subsequently, 1.0 mL of water for injection was aseptically filled in the other chamber and sealed with a rubber stopper, followed

Example 2-11-1	TMD123H L-arginine hydrochloride Polysorbate 80	30 10 0.1	W	-	-	99.2
Example 2-12-1	TMD123H D-trehalose dihydrate Polysorbate 80	30 10 0.1	W	-	-	98.8
Example 2-13-1	TMD123H L-arginine hydrochloride D-trehalose dihydrate Polysorbate 80	30 10 10 0.1	W	-	-	98.7
Example 2-14-1	TMD123H Sodium L-glutamate monohydrate D-trehalose dihydrate Polysorbate 80	30 10 10 0.1	W	-	-	98.8
Example 2-15-1	TMD123H Sodium L- glutamate monohydrate D-(-)-mannitol Polysorbate 80	30 10 10 0.1	W	-	-	99.2
Example 2-16-1	TMD123H sodium L-aspartate monohydrate D-(-)-mannitol Polysorbate 80	30 10 10 0.1	W	-	-	99.3
Example 2-17-1	TMD123H L-glutamic acid D-(-)-mannitol sodium hydroxide Polysorbate 80	30 10 10 2.8 0.1	W	-	-	99.1
Example 2-18-1	TMD123H Sodium L-glutamate monohydrate D-(-)-mannitol Polysorbate 20	30 10 10 0.1	W	-	-	97.7